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EXAMINER
SIEW, JEFFREY

ART UNIT	PAPER NUMBER
1637	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 07-01)

	Application No.	Applicant(s)
Office Action Summary	10/028,748	MACK ET AL.
	Examiner	Art Unit
	Jeffrey Siew	1656

-- *The MAILING DATE f this communicati n appears on the c ver sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2001* .

2a)☐ This action is **FINAL**.   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

    If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All b)☐ Some * c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____ .

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

    a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)   4)☐ Interview Summary (PTO-413) Paper No(s). _____ .

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)   5)☐ Notice of Informal Patent Application (PTO-152)

3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1,6* .   6)☐ Other: .

DETAILED ACTION

Priority

1.   If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. **The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application.** If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c).A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question

whether the delay was unintentional. The petition should be directed to the Office of

Petitions,Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Specification

2.   The title of the invention is not descriptive. A new title is required that is clearly

indicative of the invention to which the claims are directed.

The following title is suggested: Computer-aided display for Comparative Gene

Expression

Double Patenting

3.   The nonstatutory double patenting rejection is based on a judicially created doctrine
grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or
improper timewise extension of the "right to exclude" granted by a patent and to prevent possible
harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.
Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686
F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA
1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to
overcome an actual or provisional rejection based on a nonstatutory double patenting ground
provided the conflicting application or patent is shown to be commonly owned with this
application. See 37 CFR 1.130(b).
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal
disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37
CFR 3.73(b).

Claims 1-48 are rejected under the judicially created doctrine of obviousness-type double

patenting as being unpatentable over claims 1-50 of U.S. Patent No. 6,420,108. Although the

conflicting claims are not identical, they are not patentably distinct from each other because

claims 1-50 of US 6,420,108 are drawn to the computer method and product of displaying a

mark at X,Y displaying information in response to user input which represents a species of the

genus computer method and product claims of the instant application which are drawn to

displaying a mark.

Claim Rejections - 35 USC § 112

4.   The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for

failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention.

A)   Claims 1-48 are vague and indefinite because of the terms "position" and "relative" in

claims 1,20,25,44,47 & 48. It cannot be determined what measure is used to define the meaning

of "relative". It is suggested that position be amended to "position with X, Y coordinates where

in the X position is selected relative to the first axis and Y axis etc". For subsequent claims 19 &

43 which involve a third axis, it is suggested to add Z coordinates. The use of these terms would

have been well known and commonly practiced in the art of graphically displaying images.

B)   Claims 1-48 are vague and indefinite because of the term "corresponding". Particularly in

claims 1,20,25,44,47 & 48, it cannot be determined in what way or manner the "correspondence"

is to occur.

C)   Claim 4 recites the language "mark step" and depends on claim 1. However, proper antecedent basis is lacking in claim 1.Claim 4 depends on claim 1 which recites the language of "displaying a mark". However, claim 1 does not recite a "mark step". It cannot be determined what the term is referring to.

D)   Claim 6 recites the language " said monitoring step" and depends on claim 3. However, proper antecedent basis is lacking in claim 3. It cannot be determined to what monitoring step is being referred to.

E)   Claim 25 recites the language "first and second". However, proper antecedent basis is lacking in claim 25 for these terms. It is suggested the claims be amended to include "a first and second".

F)   Claim 6-10 are confusing because it cannot be determined to where the step of inputting is to occur. It cannot be determined whether the input is referring to the probe pair into the samples or the results into a computer for display.

G)   Claim 6 is confusing because it cannot be determined at what point the steps are to be performed in relationship to the steps in claims 1 & 6. It is suggested that a phrase be included in the preamble reciting "wherein the comparing step" further comprises".

H)   Claim 10 & 34 are confusing because of the term "pairs that cause" because it cannot be determined as to what the pairs are to cause.

I)   Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: computing the IDIF between the Ipm-Imm. Clarificaton is requested.

J)   Claim 10 &34 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: averaging the IDEF values. The specification discloses that the determination of expression is based on several calculations may be used to calculate the expression level (see page 11, lines 5-14). However in using the calculation of the sum of IDEF values as recited in claim 10 would necessitate an averaging step.

K)   Claim 11& 35 are confusing because of the phrase "user input selecting said mark" is not grammatically correct. It cannot be determined what the phrase is referring to. It is suggested the phrase be amended to " an input of a user's selection of said mark".

L)   Claims 16 & 40 are confusing because of the phrase "presence of disease". Although disease level or state are commonly used, the use of "presence" would more likely refer to an actual physical presence such as a bacteria or virus. It is suggested that the claim be amended to "disease state".

M)   Claim 30 recites the language " said monitoring step" and depends on claim 3. However, proper antecedent basis is lacking in claim 27. It cannot be determined to what monitoring step is being referred to.

Claim Rejections - 35 USC § 102

5.   The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the

basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 20,21 & 23 are rejected under 35 U.S.C. 102(b) as being anticipated Zhao et

al (Gene Vol. 156 pp. 207-213 1995).

Zhao et al teach bioimaging analyzer system to compare the expression profiles of

thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis

in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see

whole document esp. Abstract). A quantitative analysis of the filter is performed using Fuji

Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The

final part is sequence analysis in which each clone is characterized by homology search in the

GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system

for the comparative analysis of expression profile of the human cDNAs in brain. The expression

profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft

Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for

each gene is positioned relative to the expression levels in the two different samples.

Claim Rejections - 35 USC § 103

6.   The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in
> section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are
> such that the subject matter as a whole would have been obvious at the time the invention was made to a person
> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the
> manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the

claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c)

and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7.   Claims 25-29,44,45,47 & 48 are rejected under 35 U.S.C. 102(b) as anticipated by or, in

the alternative, under 35 U.S.C. 103(a) as obvious over Zhao et al (Gene Vol. 156 pp. 207-213

1995).

Zhao et al teach bioimaging analyzer system to compare the expression profiles of

thousands of genes cDNAs simultaneously . They teach a high density cDNA filter analysis in

which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see

whole document esp. Abstract). A quantitative analysis of the filter is performed using Fuji

Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The

final part is sequence analysis in which each clone is characterized by homology search in the

GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system

for the comparative analysis of expression profile of the human cDNAs in brain. The expression

profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft
Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for
each gene is positioned relative to the expression levels in the two different samples. Although
the reference is silent to the teaching of "code", it was well known and commonly practiced that
Microsoft Excel (see page 211) is a software product containing code used to generate graphs.
Through the use of this code, Zhao et al generated the graphs depicted in Figure 3 to compare the
expression level of two different samples. Moreover, the computer used was a Macintosh
computer(see page 211) as depicted in Figure 1. Although the reference is silent to the teaching
of processor, memory and display, the personal computer inherently contains a display,
microprocessor and memory in the form of RAM, ROM and hard disk.

In the alternative one of ordinary skill in the art would have been motivated to implement
the Microsoft Excel program in code format to display the expression level in order to analyze
various data inputs from various samples on different platforms. A program code provides
versatility in allowing dynamic input to be analyzed. It would have been advantageous to
implement analysis and display on code so that a large number of different samples would be
analyzed especially over time. Moreover, the implementation on code would allow the analysis
to be performed across different platforms and even different machines. It would have been
prima facie obvious to implement the display of the expression levels through a computer code
comprising code in order to analyze and display a constantly changing and new input across
different platforms and machines.

Moreover, in the alternative one of ordinary skill in the art would have been motivated to
to display the expression level on a computer system containing display, processor and memory
in order to analyze various data inputs from various samples. A computer system provides
excellent data storage and data manipulation capabilities. It would have been advantageous to
implement analysis and display on a computer system so that a large number of different samples

would be analyzed. It would have been prima facie obvious to implement the display of the expression levels on a computer system in order to analyze large amounts of data efficiently.

8.   Claim 19 & 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al (Gene Vol. 156 pp. 207-213 1995).

The teachings or suggestions of Zhao et al are described previously, briefly they teach bioimaging analyzer system to compare the expression profiles of thousands of genes cDNAs) simultaneously. They teach the a high density cDNA filter analysis in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see whole document esp. Abstract). A quantitative analysis of the filter is performed using Fuji Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The final part is sequence analysis in which each clone is characterized by homology search in the GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system for the comparative analysis of expression profile of the human cDNAs in brain. The expression profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3). A mark for each gene is positioned relative to the expression levels in the two different samples. Although the reference is silent to the teaching of "code", it was well known and commonly practiced that Microsoft Excel (see page 211) is a software product containing code used to generate graphs. Through the use of this code, Zhao et al generated the graphs depicted in Figure 3 to compare the expression level of two different samples. Moreover, the computer used was a Macintosh computer(see page 211) as depicted in Figure 1. Although the reference is silent to the teaching of processor, memory and display, it was well known and commonly practiced in the art that personal computer contains a display, microprocessor and memory in the form of RAM, ROM and hard disk.

Zhao et al do not teach a third axis.

One of ordinary skill in the art would have been motivated to apply a third axis to Zhao et al display format in order to further compare the expression level in a third sample. It would have been advantageous to use a 3D format to compare three samples at the same time so that comparisons would be visually easier to interpret and would be performed simultaneously. It would have been prima facie obvious to apply a third axis to Zhao et al's display format in order to analyze more information at the same time.

9.   Claims 6-18 & 30-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al (WO97/27317 21 July 1997) in view of Zhao et al (Gene Vol. 156 pp. 207-213 1995).

Claims 6-18 are drawn to claim 1 in which the expression level of expressed sequence is monitored.

Claims 30-42 are drawn to computer product comprising code for displaying a first axis corresponding to expression level of first axis, code for displaying a first axis corresponding to expression level of first axis and code for displaying a mark , a computer readable storage medium for storing codes.

Lockhart et al teach a method of detecting nucleic abundances or concentrations (e.g. expression levels) between two or more samples (see whole document esp. abstract). They teach the simultaneous monitoring of the expression of a multiplicity of genes using perfect match probe and mismatch probes (see page 5,12,47 & esp. 49-50). They teach that expression monitoring would be useful for both drug safety and toxicology screenings (see page 230) and monitoring various genes in response to defined stimuli such as drugs (see page 22). They teach that monitoring of gene expression may be performed using a computer system running a software program that includes computer code incorporating analysis of hydridization intensities

of the screens(see page 90 & Figure 6-8). They teach a method of comparing expression level

using the hybridization intensities between the perfect match and mismatch probes (see page 93-

101 & Figure 9-10B). They compare the hybridization intensity difference and ratio of the

perfect match and mismatch probes with a threshold. The values NPOS, NNEG and LR are

calculated for each pair of probes. The analysis is repeated to calculate the average of the

differences. They teach that oligonucleotide pairs that show the greatest differential hybridization

between two samples can be identified by sorting the observed hybridization ratio and difference

values. Based on identified oligonucleotide pair sequences, a gene can be searched for in

sequence databases such as GENBANK (see page 128-9). They also display the results in a

graph showing differential expression between samples (see Figures 16-17).

Lockhart et al do not teach presenting expression level information by displaying on a

first axis representing the expression level in a first sample, displaying on second axis

representing the expression level in the second axis and displaying a mark relative to the two

axes.

Zhao et al teach bioimaging analyzer system to compare the expression profiles of

thousands of genes cDNAs) simultaneously . They teach the a high density cDNA filter analysis

in which expression profiles of 2505 cloned human brain cDNAs (genes) were monitored (see

whole document esp. Abstract). A quantitative analysis of the filter is performed using Fuji

Bioimaging Analyzer BAS2000 System and automated quantification program AutoQuant. The

final part is sequence analysis in which each clone is characterized by homology search in the

GENBANK nucleotide Sequence Database (see page 208 & Figure 1). They applied the system

for the comparative analysis of expression profile of the human cDNAs in brain. The expression

profiles were illustrated on graphs by comparing the their scores from two tissues with Microsoft

Excel (Microsoft) on a Macintosh personal computer(see page 210-211 and fig. 3).

One of ordinary skill in the art would have been motivated to display the comparative

expression levels of genes as in Zhao et al's to Lockhart et al's analysis technique in order to

compare the gene expression between two different samples. Zhao et al's display format allows

easy visualization of the many different expressions of genes between two samples. It would

have been prima facie obvious to construct a graph with an axis representing the gene expression

in one sample and another axis representing the gene expression in a second sample in order to

compare the differential gene expression between the different samples.

10.   Claims 22, 24 & 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao

et al in view of Beattie (US5,843,767 December 1, 1998).

Claims 22 & 24 are drawn to claim 20 with the added limitation the polymer is a protein.

Claim 46 is drawn to claim 44, a computer product with the added limitation the polymer

is a protein.

The teachings and suggestions of Zhao et al are described above.

Zhao et al do not teach the use of protein polymers.

Beattie et al teach the use of protein probes such as antibodies in hybridization array (see

whole document).

One of ordinary skill in the art would have been motivated to apply Beattie et al's

teaching of using protein probes to Zhao et al's expression display in order to compare the

expression level of actual translated protein between two samples. Beattie states that the use of

antibodies or ligand receptor binding would be applicable to the study of identifying

biomolecules. It was well known and commonly practiced to use these ligand -receptor binding

techniques in order to actually identify the stage of gene expression i.e. the translated protein. It

would have been prima facie obvious to use Beattie's protein probes and display the results

between two samples using Zhao et al's expression method in order to compare the protein

levels which represent the final stage of gene expression.

SUMMARY

11.   No claims allowed.

CONCLUSION

13.   Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and

whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security

through the e-mail system nor should official papers be transmitted through this route. The

examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can

be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this

application or proceeding should be directed to the Tracey Johnson for Art Unit 1637 whose

telephone number is (703)-305-2982.

Papers related to this application may be submitted to Group 1600 by facsimile

transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal

Mall 1. The faxing of such papers must conform with the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice

(703) 308-3290 and Before Final FAX (703) 872-9306 or After Final FAX (703) 30872-9307.

JEFFREY SIEW
PRIMARY EXAMINER

January 12, 2003